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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,384	11/03/2005	Paul Leonard Greenhaff	SWIN 3306	5375

7812 7590 12/15/2009

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
12/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,384	GREENHAFF ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 9/25/2009 has been entered.

The Request for Continued Examination filed 9/25/2009 has been carefully considered. The following information has been made of record in the RCE filed for the instant application:

1. Claims 1-57 have been canceled.

2. Claims 58-67, 71-73, 77-84, 88-90, 93-94, 96-103, 109 and 111 have been amended.

Claims 58-111 are pending in the case.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58-66, 68-83, 85-102 and 104-111 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising L-carnitine and glucose, sucrose or fructose and the method of increasing carnitine retention using the said composition, does not reasonably provide enablement for a composition comprising any other agent and its use in the method as instantly claimed. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention
(2) The state of the prior art
(3) The relative skill of those in the art
(4) The predictability or unpredictability of the art
(5) The breadth of the claims
(6) The amount of direction or guidance presented
(7) The presence or absence of working examples; and
(8) The quantity of experimentation necessary.

The most relevant factors are discussed below.

The nature of the invention

The instant invention pertains to compositions comprising a carnitine substance and an agent to increase blood/plasma insulin concentration and method of increasing carnitine retention in animal or human skeletal muscle using the said composition.

The breadth of the claims

Instant claims 58, 63, 93, 99 and dependent claims thereof recite the terms, an agent to increase blood/plasma insulin concentration and carbohydrates, proteins and amino acids. The recitation, 'an agent to increase blood/plasma insulin concentration' is functional language. The recitations are broad and are seen to include any substance as agent and any carbohydrate, protein or amino acid including synthetic proteins.

The amount of direction provided or guidance presented by the inventor

The instant specification (page 5, 15-18) teaches that the agent can be carbohydrate or a derivative of carbohydrate but the claim recitation is seen to include substances other than carbohydrates. Even the term carbohydrate is broad and is seen to include any carbohydrate. Proteins and amino acids are not seen in the definition. The amounts recited for the agents are also very high.

The level of Predictability or Unpredictability in the Art

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed. Prior art used in the rejections below, teaches the use of L-carnitine, its acyl derivative, amino acids and ribose in addition to glucose, fructose and sucrose. The art is silent regarding the use of any sugar/carbohydrate and protein. Based on the teachings of the prior art it is highly unpredictable that the instant compositions comprising any carbohydrate and protein in the high amounts recited can be used in the methods as instantly claimed. The instantly claimed invention is highly unpredictable.

The presence or absence of working examples

The working examples set forth in the instant specification are drawn to the use of L-carnitine and glucose as the agent. One of ordinary skill in the art will not be able to figure out what other carbohydrates and proteins can be used in the instant composition to perform the functions as claimed. Thus, the specification fails to provide clear and convincing evidence in sufficient support of for the active agents and their use in the method as recited in the instant claims. As a result, it necessitates one of skill to perform an exhaustive search for the embodiments of using any carbohydrate or protein as recited in the instant claims suitable to practice the claimed invention.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the compositions and methods of use as broadly encompassed by the recitation in the instant claims. One of ordinary skill in the art would have to carry out undue experimentation to practice the instant invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation*, with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 58 recites, 'carnitine substance'. It is not clear what all are encompassed by the term substance. The specification (page 5, 9-13) defies the said terms as L-carnitine, a functional equivalent of carnitine, an active derivative of carnitine or carnitine analogue. Other than L-carnitine the rest of the terms used in the definition are also broad. The metes and bounds are unclear. Therefore, the scope of the claim is indefinite as to what the term 'carnitine substance' encompasses. This also applies to all other claims in which the said terms are recited. Claim 58 also recites the terms, 'an agent'. The specification (page 5, 15-18) teaches that the agent can be carbohydrate or a derivative of carbohydrate but the claim recitation is seen to include substances other than carbohydrates. The metes and bounds of the term derivative is also unclear.

The term "simple" in claim 65 is a relative term which renders the claim indefinite. The term "simple" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification gives examples of simple carbohydrates but the degree of simplicity is not clear from these examples either. The said term is also recited in other claims.

Claim 94 recites the term derivative. In the absence of the specific derivatizations to the chemical core claimed or distinct language to describe the structural modifications or the

chemical names of the derivatives of this invention, the identity of said derivatives would be difficult to define and the metes and bounds of the said derivatives applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claim(s).

Claims 59-64 and 66-93 and 95-111 which depend from rejected base claims that are unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 58-63, 76-80 and 91-92 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al (EP 0680945, of record).

Davis teaches compositions comprising carnitine, glycine which is useful for carnitine absorption (amino acid; the agent; pages 5-6; Examples 1-7; limitations of claims 58-63; page 3, lines 16-21. Davis discloses the said composition in the form of an aqueous solution (page 3, lines 48-50; limitations of claims 74-80 and 91-92).

Claims 58-65, 74, 76-83, 91 and 93-102 are rejected under 35 U.S.C. 102(b) as being anticipated by Pola (WO 01/95915, of record).

Pola teaches a food/dietary supplement comprising L-carnitine and acyl derivatives of L-carnitine and Ribose (a simple sugar; pages 6-9; pages 11-14; limitations of claims 58-65, 76-83). The composition can be in the form of syrup (page 12, line 3; limitations of claims 74, and 91). Pola teaches the administration of a solution comprising his composition to rats via injection. The results of this test shows that carnitine is absorbed by the tissue as evidenced by the number of ectopic contractions observed (page 5, Experimental through page 6, Table 2; limitations of claims 93-102).

Claims 93-103 are rejected under 35 U.S.C. 102(b) as being anticipated by Bohles et al (J. Parenteral and Enteral Nutrition, 1984, 8(1), 9-13, of record).

Bohles teaches a method increasing carnitine retention by administration of amino acids, glucose (both insulin increasing agents) and L-carnitine to piglets (page 9, abstract and right column, see under Experimental Design). The administration is seen to produce increased energy gain and improvement in nitrogen balance, all of which indicate carnitine retention. This teaching is seen to meet the limitations of instant claims 93-103.

Claims 93-103 are rejected under 35 U.S.C. 102(b) as being anticipated by Gross et al (Biochim. Biophys. Acta., 1993, 1170(3), 265-274, of record).

Gross teaches the uptake and retention of carnitine by rats (abstract, page 266, right column, section entitled-Intestinal levels of carnitine trough page 267). The study also deals with sodium dependent uptake. This teaching is seen to meet the limitations of instant claims 93-103.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 63-73, 84-90 and 104-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al (EP 0680945, of record) in view of Pola (WO 01/95915, of record), Bohles et al (J. Parenteral and Enteral Nutrition, 1984, 8(1), 9-13; cited in IDS of 11/3/2005) and Gross et al (Biochim. Biophys. Acta., 1993, 1170(3), 265-274).

The teaching of Davis, Pohles, Pola and Gross is explained above. However, the prior art above do not teach the use of carbohydrate derivatives, proteins, other sugars like fructose or derivatives thereof and the amounts of carnitine and the agent as instantly claimed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make composition including food supplements comprising carnitine or its derivatives, proteins and sugars like fructose and sugars and use them in a method of increasing carnitine retention since closely analogous compositions comprising carnitine and the additional agent to increase or stimulate insulin level is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make the compositions as instantly claimed and use them in a method as instantly claimed since carnitine uptake and retention is shown in animals and suggested for humans (Gross et al, page 274, right column) and Pola teaches synergistic effect of carnitine and its derivatives (acyl derivatives) and ribose sugar combination on myocardial insufficiency and muscle fatigue. Pola also suggests a 1:10 ratio of carnitine to ribose (page 3, line 2; and lines 3-17). One of skill in the art would look for other such combinations. It is well within the skill level of the artisan to adjust the amounts of the active agents in order to optimize the beneficial effects.

Response to Applicants Arguments

Applicants have not filed any new Remarks/Arguments with the filing of the instant RCE. Hence, the Examiner's response is with regard to their arguments filed 1/12/2009 (Applicants response to the first Non-final action in this application).

Applicants have traversed the rejection arguing that:

1. The composition of Davis is to stimulate the absorption of carnitine across the intestinal cell wall. This is very different from the instant claims which relate to increasing carnitine retention in skeletal muscle. The uptake of carnitine into skeletal muscle is very different from absorption across the gut wall. Simply increasing the amount of carnitine blood/plasma does not increase carnitine retention in skeletal muscle.

2. Pola teaches a supplement comprising ribose or its phosphorylated analog and a carnitine substance. Ribose does not stimulate insulin production.

3. Bohles discloses administration of carnitine with glucose and the insulin level was reduced.

4. Gross is concerned with carnitine retention in the intestine and not in the skeletal muscle.

Applicants' arguments have been considered but are not found to be persuasive.

Davis teaches compositions comprising carnitine and glycine, which is useful for carnitine absorption (glycine, an amino acid: the agent to increase insulin concentration as in instant claims 58 and 63; pages 5-6; Examples 1-7; limitations of claims 58-63; page 3, lines 16-21). Davis discloses the said composition in the form of an aqueous solution (page 3, lines 48-50).

Gross teaches the uptake and retention of carnitine by rats (abstract, page 266, right column, section entitled-Intestinal levels of carnitine trough page 267). The study also deals with sodium dependent uptake. Gross may not have specifically taught carnitine retention in skeletal muscle. But his teaching still deals with carnitine retention in body tissue.

Bohles teaches a method increasing carnitine retention by administration of amino acids, glucose (both insulin increasing agents) and L-carnitine to piglets (page 9, abstract and right column, see under Experimental Design). The administration is seen to produce increased energy gain and improvement in nitrogen balance, **all of which indicate carnitine retention**. Applicants argue that the administration of carnitine with glucose shows a decrease in insulin levels as shown in Table II, period 3 (page 11). According to Bohles (page 9, Experimental Design) during period 3 part of glucose was substituted with fat. During period 1 only glucose was fed. In Table II it can be seen that during period 1, when only glucose was fed insulin level is high. During period 3 the insulin level is low which is to be expected since the amount of glucose intake has been reduced. So, as long as glucose is intake is there it is going to increase the insulin level and will also help with the retention of carnitine.

Pola teaches a food/dietary supplement comprising L-carnitine and acyl derivatives of L-carnitine and Ribose (a simple sugar; pages 6-9; pages 11-14; limitations of claims 58-65, 76-83). The composition can be in the form of syrup (page 12, line 3; limitations of claims 74, and 91). Pola teaches that his composition is an effective supplement for prevention of skeletal muscle dysfunction (page 2, second full paragraph) and for energy supply during prolonged physical activity and muscle fatigue. **In order for carnitine to perform this function it must be absorbed and retained in the skeletal muscle**. Even though ribose may not be taught to increase insulin levels Davis teaches the use of glycine, an amino acid (as instantly claimed) for carnitine absorption and Bohles teaches (and has also demonstrated as explained above) the use of glucose, which increases insulin level. Hence, one of ordinary skill in the art based on the teaching of Bohles and Pola would use a composition comprising carnitine and a carbohydrate

like glucose that increases insulin level, in a method to increase carnitine retention. This is suggested mainly by the teachings of Boles and Pola. The instant claims are rendered obvious by the prior art.

Conclusion

Claims 58-111 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
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